

AMENDMENTS TO THE CLAIMS

Please amend claims 1, 21, 47, and 48 without prejudice or disclaimer. The following listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A process for producing a blood plasma-derived l α lp composition comprising a mixture of inter-alpha inhibitor protein (I α I) and pre-alpha protein (P α I), wherein the I α I and the P α I are present in said mixture in a physiological proportion, the process comprising:
isolating from blood plasma a plasma fraction containing I α I and P α I, wherein the I α I and P α I are present in a physiological proportion; and
purifying the plasma fraction to obtain an l α lp composition with a purity of l α lp ranging from about 85% to about 100% pure, wherein the purifying comprises hydroxylapatite chromatography.
2. (Previously presented) The process of claim 1, wherein the isolating comprises solid phase extraction or chromatographing blood plasma.
- 3-9. (Canceled)
10. (Previously presented) The process of claim 1, wherein the plasma fraction comprises a side fraction obtained from the purification of clotting factor IX or from the purification of a prothrombin complex concentrate.
11. (Canceled)
12. (Previously presented) The process of claim 1, wherein the plasma fraction is isolated as a cryosupernatant resulting from cryoprecipitation of blood plasma.
13. (Previously presented) The process of claim 1, wherein the plasma

fraction is cryo-poor plasma.

14. (Previously presented) The process of claim 1, wherein the plasma fraction is human, primate, bovine, porcine, feline, or canine.

15. (Previously presented) The process of claim 1, further comprising obtaining blood, obtaining blood plasma, obtaining a side fraction obtained from the purification of clotting factor IX, obtaining a side fraction from the purification of a prothrombin complex concentrate, obtaining a cryosupernatant resulting from cryoprecipitation of blood plasma or obtaining cryo-poor plasma.

16-20. (Canceled)

21. (Currently amended) The process of claim 1, wherein the purifying ~~comprises is by hydroxylapatite chromatography, affinity chromatography or a combination thereof.~~

22-24. (Canceled)

25. (Previously presented) The process of claim 1, wherein the Ial and Pal present in the plasma fraction have an apparent molecular weight of between about 60,000 to about 280,000 kDa.

26. (Canceled)

27. (Previously presented) The process of claim 1, further comprising: further purifying the plasma fraction; virus inactivating the plasma fraction and/or the purified Ialp; the addition of stabilizers; comprising pasteurization of the purified Ialp; or anion-exchange chromatography of the purified Ialp.

28. (Previously presented) The process of claim 27, wherein the further

purifying the plasma fraction is by passing through heparin affinity column and collecting the flow through (unbound) fraction; the virus inactivating is by a solvent/detergent treatment or thermal inactivation; and the anion-exchange chromatography of the purified lalp is diethylaminoethyl (DEAE) Sepharose.

29-30. (Canceled)

31. (Previously presented) The process of claim 28, wherein the thermal inactivation comprises pasteurization at a temperature of between about 55 to about 65°C. or dry heat at 70 to 120°C.

32-39. (Canceled)

40. (Previously presented) A composition of lalp comprising a mixture of inter-alpha inhibitor protein (Ial) and pre-alpha protein (Pal), wherein the Ial and the Pal are present in said mixture in a physiological proportion ranging from about 85% to about 100% pure.

41. (Original) The composition of claim 40, wherein the lalp comprises between about 60% to about 80% Ial and between about 40% to about 20% Pal.

42. (Original) The composition of claim 40, wherein the physiological proportion is the ratio of Ial to Pal that appears naturally in human plasma.

43-44. (Canceled)

45. (Original) The composition of claim 40, further comprising a stabilizing agent.

46. (Original) The composition of claim 45, wherein the stabilizing agent is albumin, polyethylene glycol, alpha,alpha-trehalose, amino acids, salts, glycerol,

omega-amino acids, sugar, or combinations thereof.

47. (Currently amended) A composition of lalp comprising a mixture of inter-alpha inhibitor protein (Ial) and pre-alpha protein (Pal), wherein the Ial and the Pal are present in said mixture in a physiological proportion and: have a high trypsin inhibitory specific activity between about 1000 to about 2000 IU/mg; have a half life of greater than one hour; comprise a light chain of inter-alpha inhibitor protein associated with at least one of three heavy chains H1, H2 and H3; or comprise a light chain of inter-alpha inhibitor protein associated with at least one of three heavy chains H1, H2, H3 and H4.

48. (Currently amended) The composition of claim 47, wherein the ~~the~~ trypsin inhibitory specific activity is between about ~~1000~~ 1400 to about 2000 IU/mg.

49-55. (Canceled)

56. (Previously presented) The composition of claim 47, wherein the lalp composition has a half life of at least 5 hours.

57. (Previously presented) The composition of claim 47, wherein the lalp composition has a half life of at least 10 hours.

58-76. (Canceled)

77. (Previously presented) A composition of lalp comprising a mixture of inter-alpha inhibitor protein (Ial) and pre-alpha protein (Pal), wherein the Ial and the Pal are present in said mixture in a physiological proportion, said composition having been prepared by the process according to claim 1.

78. (Previously presented) The composition of claim 40, further comprising an

additional therapeutic agent.

79. (Original) The composition of claim 78, wherein the additional therapeutic agent is an anticancer agent, an anti-inflammatory agent, an anti-coagulant or an immunomodulator.

80. (Previously presented) A pharmaceutical composition comprising a therapeutically effective amount of the composition of claim 40, and a pharmaceutically acceptable carrier.

81. (Previously presented) A method of treating an inflammation related disorder, cancer, or an infectious disease in a subject comprising, administering a therapeutically effective amount of the composition of claim 40 or 77.

82. (Canceled)

83. (Canceled)

84. (Original) The method of claim 81, wherein the lalp is administered as a tablet, capsule, or injectables.

85. (Canceled)

86. (Canceled)

87. (Canceled)

88. (Withdrawn) A method of treating a subject for acute inflammatory disease, sepsis, severe shock, septic shock, rheumatoid arthritis, cancer, cancer metastasis, infectious disease, or preterm labor, comprising:

(a) determining the pre-treatment level of one or more of the following levels in a subject:

- (i) the level of $\text{I}\alpha\text{I}$;
- (ii) the level of $\text{P}\alpha\text{I}$;
- (iii) the level of $\text{I}\alpha\text{I}\text{p}$;
- (iv) the level of H3;
- (v) the level of H4;
- (vi) the level of H1;
- (vii) the level of H2; and
- (viii) the level of LC; and

(b) administering a therapeutically effective amount of the composition of claim 40 or 77 to the subject.

89-95. (Canceled)

96. (Withdrawn) A method for predicting a response to an $\text{I}\alpha\text{I}\text{p}$ therapy, comprising:

assaying a sample obtained from a subject to detect the level of one or more of the following:

- (i) $\text{I}\alpha\text{I}$;
- (ii) $\text{P}\alpha\text{I}$;
- (iii) $\text{I}\alpha\text{I}\text{p}$;
- (iv) H3;
- (v) H4;
- (vi) H1;
- (vii) H2; and

(viii) LC; wherein the detected levels identifies a subject that may respond favorable to $\text{I}\alpha\text{I}\text{p}$ therapy.

97. (Canceled)

98. (Withdrawn) A method of monitoring the progress of a subject being treated with an lalp therapy, comprising:

(a) determining the pre-treatment level of one or more of the following levels, in a subject:

- (i) the level of lal;
- (ii) the level of Pal;
- (iii) the level of lalp;
- (iv) the level of H3;
- (v) the level of H4;
- (vi) the level of H1;
- (vii) the level of H2; and
- (viii) the level of LC;

(b) administering a therapeutically effective amount of the composition of claim 40 or 77 to the subject; and

(c) determining the level of one or more of the levels in the subject after an initial period of treatment with the composition,

wherein an increase of the level in the subject following treatment with the composition indicates that the subject is likely to have a favorable clinical response to treatment with lalp.

99. (Withdrawn) A kit for lalp therapy comprising one or more of the following:

- (i) lal;
- (ii) Pal;
- (iii) lalp;
- (iv) H3;
- (v) H4;
- (vi) H1;
- (vii) H2; and
- (viii) LC; and

instructions for therapeutic use.

100. (Canceled)

101. (Previously presented) A kit comprising a composition according to claim 40 or 77 and instructions for therapeutic use.